REMARKS:

Claims 1, 2, 4-11, 13, 16, 18, 19, 24, 27, 28, 30-37, 39, 43, 45, 46, 51 and 104-107 are presented for examination. Claims 1, 2, 4, 27, 28, 30 104, 105, 106 and 107 have been amended hereby. Claims 12, 14, 15, 17, 20-23, 25, 26, 38, 40-42, 44, 47-50, 52-103 and 108-111 are withdrawn (without prejudice or disclaimer). Claims 3 and 29 are cancelled (without prejudice or disclaimer).

Initially, regarding claims 4 and 30, it is noted that these claims have been amended hereby to recite "wherein the demineralized bone matrix is selected from the group of: (a) an osteoinductor; and (b) an osteoconductor".

As described in the specification at page 2, line 31 to page 3, line 2, an "osteoinductive material" includes "DBM". In addition, as described in the specification at page 3, lines 3-9, an "osteoconductive material" includes "DBM".

Thus, since DBM is included as an osteoinductive material and as an osteoconductive material, and since claims 4 and 30 have been amended hereby to recite "wherein the demineralized bone matrix is selected from the group of: (a) an osteoinductor; and (b) an osteoconductor", it is respectfully submitted that these claims 4 and 30 are properly presented for examination.

Reconsideration is respectfully requested of the rejection of claims 1, 2, 5-11, 13, 16, 18, 19, 24, 27, 28, 31-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement (of note, it is believed that claims 4 and 30 are properly presented for examination; in addition, it is noted that the cancellation of claims 3 and 29 has rendered their rejection moot).

Applicants do not necessarily concur with the Examiner with regard to support for the range as previously claimed.

Nevertheless, in an effort to expedite prosecution of the present application, independent claims 1, 27, 104 and 106 have been amended hereby to more clearly recite subject matter supported by the specification.

More particularly, each of independent claims 1, 27, 104 and 106 has been amended hereby to recite the following:

- "wherein a weight of the demineralized bone matrix ranges from about 20% to about

40% of the composition by weight"

In this regard, the Examiner's attention is directed to the specification at page 29, lines 1-9, for example, which clearly provides support for the currently claimed range:

- "Human DBM provided by an AATB accredited tissue bank, Tissue Banks International (TBI, Batch No. SF9904005045, San Rafael, Calif.) was aseptically processed and freeze-dried. The average particle size of DBM was in the range of 125 to 1000μ. The sterile carrier provided by Focal, Inc. (Lexington, Mass.) was a polyethylene glycol based macromer with molecular weight of 20,000. DBM powders were mixed with a 10 wt % macromer solution in sterile phosphate buffer at three concentrations: 20, 30 and 40% by weight. Controls included TBI DBM alone and macromer carrier alone. All materials were pre-loaded into sterile gelatin capsules (size #5, Batch No. 07.039.90, Torpac, Inc. Fairfield, N.J.) (15 mg sample/capsule) and stored at -20^0 C. until surgery." (emphasis added)

Therefore, it is respectfully submitted that the rejection of claims 1, 2, 5-11, 13, 16, 18, 19, 24, 27, 28, 31-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §112, first paragraph, has been overcome.

Regarding the rejection of claims 3 and 29 under 35 U.S.C. §112, second paragraph, it is noted that the cancellation of claims 3 and 29 has rendered their rejection moot.

Reconsideration is respectfully requested of the rejection of claims 1, 2, 5-11, 13, 16, 18, 19, 24, 27-28, 31-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §103(a) as allegedly being unpatentable over WO 98/12243, hereinafter "Jarrett et al." in view of Utilization of type I collagen gel, demineralized bone matrix, and bone morphogenetic protein-2 to enhance autologous bone lumbar spinal fusion, hereinafter "Helm et al." or The use of Demineralized Bone Matrix in the Repair of Segmental Defects, hereinafter "Bolander et al." (of note, it is believed that claims 4 and 30 are properly presented for examination; in addition, it is noted that the cancellation of claims 3 and 29 has rendered their rejection moot).

The Examiner acknowledges (at page 7 of the June 9, 2008 Office Action) that "the carrier composition of Jarret does not contain demineralized bone matrix material".

Thus, in an attempt to cure this acknowledged deficiency of Jarrett et al. to disclose this feature of the claimed invention directed to use of demineralized bone matrix, the Examiner cites Helm and Bolander et al.

More particularly, the Examiner asserts (at page 7 of the June 9, 2008 Office Action) that "it is known in the art that demineralized bone matrix is used for bone repair according to Helm and Bolander".

Finally, the Examiner concludes (again, at page 7 of the June 9, 2008 Office Action) with the assertion that "taking the general teachings of the prior art, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that inclusion of demineralized bone matrix in the composition of Jarrett et al. would effectively repair bone" (the Examiner had earlier, at page 6 of the June 9, 2008 Office Action, cited Jarrett et al. at page 25, lines 11 and 12 regarding use for bone repair).

Applicants respectfully submit that the Examiner is simply using **impermissible hindsight** in constructing a hypothetical combination utilizing demineralized bone matrix.

More particularly, applicants note that many materials **besides** demineralized bone matrix are conventionally used or contemplated for bone repair.

In this regard, one of the inventors (Steve Lin) performed a search on the "PubMed" database on or about December 4, 2008. A printout of the search results is attached as Exhibit A. As seen from this Exhibit A, the keywords "Bone Graft Substitutes" returned 1,902 citations. Of these 1,902 citations, only 147 included the keywords "Demineralized Bone Matrix (DBM)". The bulk of the citations were related to citations directed to **other** bone repair mechanisms.

See also, attached Exhibit B, which provides a listing of fifteen sample articles from the "PubMed" database search demonstrating that different classes of biometarils in different physical forms were investigated for their potential as bone repair materials or clinically used to or in bone defect repair.

See also, attached Exhibit C, which shows various classes of biomaterials used in bone repair (one of the inventors (Steve Lin) generated this Exhibit C on or about December 4, 2008).

Finally, see also, attached Exhibit D, which shows a list of bone void fillers that are cleared by the FDA for bone repair -- it is believed that FocalSeal can be used with most of these products to improve handling and delivery (one of the inventors (Kurt Sly) generated this Exhibit D on or about December 4, 2008).

Thus, in view of the many materials **besides** demineralized bone matrix that are conventionally used or contemplated for bone repair, it is respectfully submitted that the Examiner's hypothetical construction is simply the result of **impermissible hindsight.**

Moreover, it is noted that a specific demineralized bone matrix weight percentage is currently claimed.

In this regard, while the Examiner points out that Jarrett et al. states (at page 25, lines 11-13) "In orthopedic surgery, uses include tendon repair, bone repair, including filling of defects, and meniscus repair," it is noted that the preceding heading (at page 24, line 24) was "Sealing Leaks in Tissue".

Thus, the "bone repair" of Jarrett et al. would appear to be related to such sealing leaks in tissue (this is supported by the indication in Jarrett et al. at page 1, lines 4-6, for example, where it is indicated that "The present invention relates to improved photopolymerizable biodegradable hydrogels for use as tissue adhesives, coatings, sealants and in controlled drug delivery devices").

Moreover, it is noted that Jarrett et al. indicates (at page 27, lines 2-4, for example) that "Another preferred application involves locally applying an incorporated agent, such as a prophylactic, therapeutic or diagnostic agent, to tissue surfaces of a patient" (this indication is made under the heading "Controlled delivery of incorporated agents" at line 1 of page 27).

As best understood, it is well known in the drug delivery art to provide an active ingredient at a relatively low level (in this regard, see, for example, U.S. Patent 7,022,343 – showing drug delivery of e.g., amiodarone).

Thus, it is believed that to the extent that one of ordinary skill in the art would assign an active ingredient percentage to Jarrett et al., such percentage would likely be under 10% (if not even lower).

In contrast, the claims now recite that the demineralized bone matrix (acting in this case as the "active ingredient") is about 20% to about 40% of the composition by weight.

In addition, it is noted that claims 5-7 and 31-33 recite that the composition is resorbed and replaced by new bone substantially throughout the volume of the composition.

It is believed that this feature even further distinguishes from the disclosure of Jarrett et al. (e.g., related to the controlled release of drugs).

Therefore, it is respectfully submitted that the rejection of claims 1, 2, 5-11, 13, 16, 18,

19, 24, 27-28, 31-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §103(a) as allegedly being unpatentable over Jarrett et al. in view of Helm et al. or Bolander et al. has been overcome.

Accordingly, it is respectfully submitted that each rejection raised by the Examiner in the June 9, 2008 Office Action has been overcome and that the above-identified application is now in condition for allowance.

Additionally, it is noted that this Amendment is fully supported by the originally filed application and thus, no new matter has been added. For this reason, the Amendment should be entered.

For example, support for the amendments to claims 1, 27, 104 and 106 regarding wherein the carrier comprises a solution of a macromer may be found in the specification as follows:

- "The applicants have found that one suitable carrier is the FocalSeal®-S sealant, available from Genzyme Corp., Cambridge, Mass., USA. It is the applicants understanding that the FocalSeal®-S sealant is an aqueous solution containing a macromer of PEG, trimethylene carbonate (TMC) and poly(lactic acid), with acrylic ester end groups. As set forth above, the composition may or may not include an initiator, such as a photoinitiator." (page 19, lines 2-6) (emphasis added)

- "Human DBM provided by an AATB accredited tissue bank, Tissue Banks International (TBI, Batch No. SF9904005045, San Rafael, Calif.) was aseptically processed and freeze-dried. The average particle size of DBM was in the range of 125 to 1000μ. The sterile carrier provided by Focal, Inc. (Lexington, Mass.) was a polyethylene glycol based macromer with molecular weight of 20,000. DBM powders were mixed with a 10 wt % macromer solution in sterile phosphate buffer at three concentrations: 20, 30 and 40% by weight. Controls included TBI DBM alone and macromer carrier alone. All materials were pre-loaded into sterile gelatin capsules (size #5, Batch No. 07.039.90, Torpac, Inc. Fairfield, N.J.) (15 mg sample/capsule) and stored at -20^0 C. until surgery." (page 29, lines 1-9) (emphasis added)

Further, support for the amendments to claims 1, 27, 104 and 106 regarding wherein a weight of the demineralized bone matrix ranges from about 20% to about 40% of the

composition by weight may be found, for example, in the specification as follows:

- "Human DBM provided by an AATB accredited tissue bank, Tissue Banks International (TBI, Batch No. SF9904005045, San Rafael, Calif.) was aseptically processed and freeze-dried. The average particle size of DBM was in the range of 125 to 1000μ. The sterile carrier provided by Focal, Inc. (Lexington, Mass.) was a polyethylene glycol based macromer with molecular weight of 20,000. DBM powders were mixed with a 10 wt % macromer solution in sterile phosphate buffer at three concentrations: 20, 30 and 40% by weight. Controls included TBI DBM alone and macromer carrier alone. All materials were pre-loaded into sterile gelatin capsules (size #5, Batch No. 07.039.90, Torpac, Inc. Fairfield, N.J.) (15 mg sample/capsule) and stored at -20^0 C. until surgery." (page 29, lines 1-9) (emphasis added)

Favorable reconsideration is earnestly solicited.

Respectfully submitted,
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